

CTCGAGGACAGTGACCTGGGAGTGAGTACAAGGTGAGGCCACCACTCAGGGT  
 GCCAGCTCCAAGCGGGTCACAGGGACGAGGGCTGCGGCCATCAGGAGGCCCT  
 GCACACACATCTGGGACACGCGCCCCGAGGGCCAGTTCACCTCAGTGCGCC  
 TCATTCTCCTGCACAAAAGCGCCCCATCCTTCTTACAAGGCTTCGTGG  
 AAGCAGAGGCAGTCGATGCCAGTACCCCTCCCTCCAGGCAACGGGACC  
 CCAAGTTGCTGACTGGGACCAAGCCACGCATGCGTCAAGAGTGAGAGT  
 CCGGGACCTAGGCAGGGCCCTGGGTTGGGCCTGAGAGAGAAGAGAACCTC  
 CCCCAGCACTCGGTGTGCATCGTAGTGAAGGAGCCTCACCTGACCCCCGCT  
 GTTGCTCAATCGACTTCCAAGAACAGAGAGAAAAGGAACTTCCAGGGCGG  
 CCCGGGCCTCCTGGGGTTCCCACCCATTAGCTGAAAGCACTGAGGCA  
 GAGCTCCCCCTACCCAGGCTCCACTGCCCGCACAGAAATAACAACCACGGT  
 TACTGATCATCTGGGAGCTGTCCAGGAATT

## FIG.\_1A

1 GCTGGGCTAA ACTGGGCTAG CCTGAGCTGG GCTGAACCTGG GCTGCTGGC  
 51 TGGACTGGGT AAGCTGGGCT GAGCTGGGTT GGGTGGAAAT GGGCTGAGCT  
 101 GAGCTAGGCT AAACTGGGTT TGGCTGGGCT GGGCTGGGCT GGG

## FIG.\_2B

1 GGTTTGGCTG GGCTGGGCTG GGCTGGGCTG GGTCAGCTG AGCGGGTTGG  
 51 GTTAGACTGG GTCAAACCTGG TTCAGC

## FIG.\_2C

## GERMLINE &amp; LOCUS

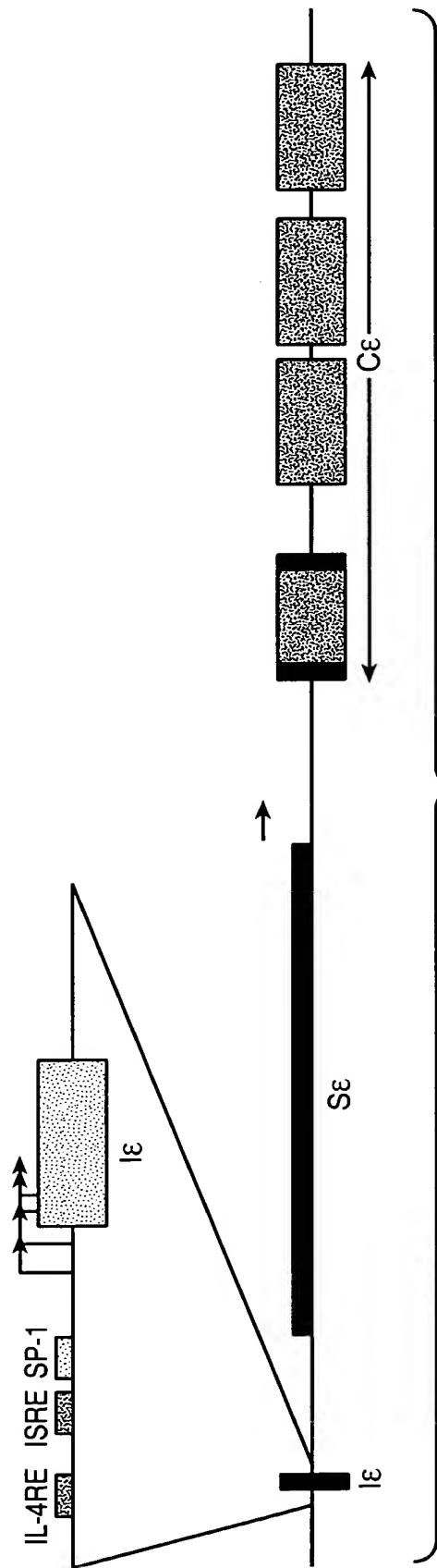


FIG. 1B

+

LOW ENERGY DNA FOLDING OF THE S<sub>E</sub> REGION

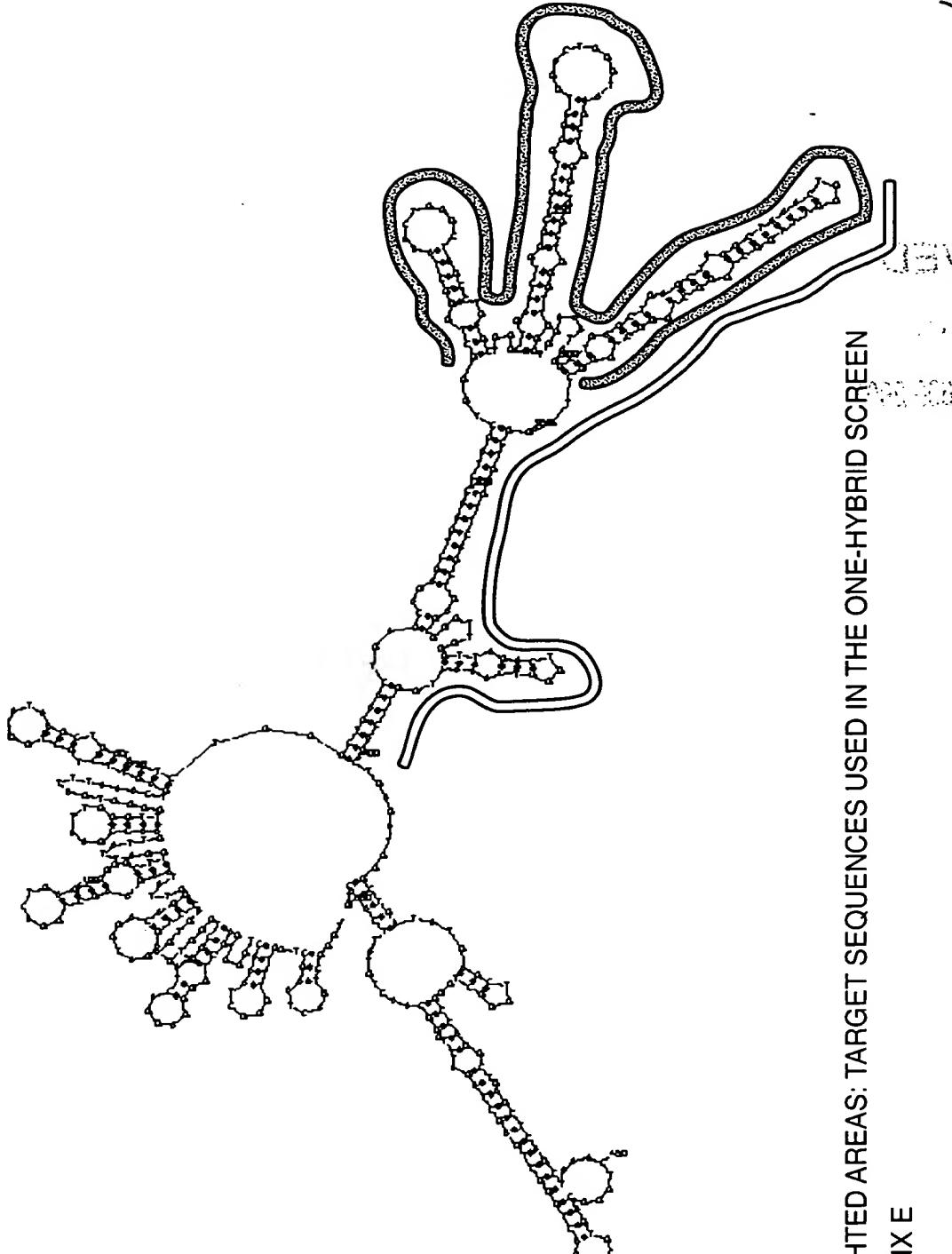
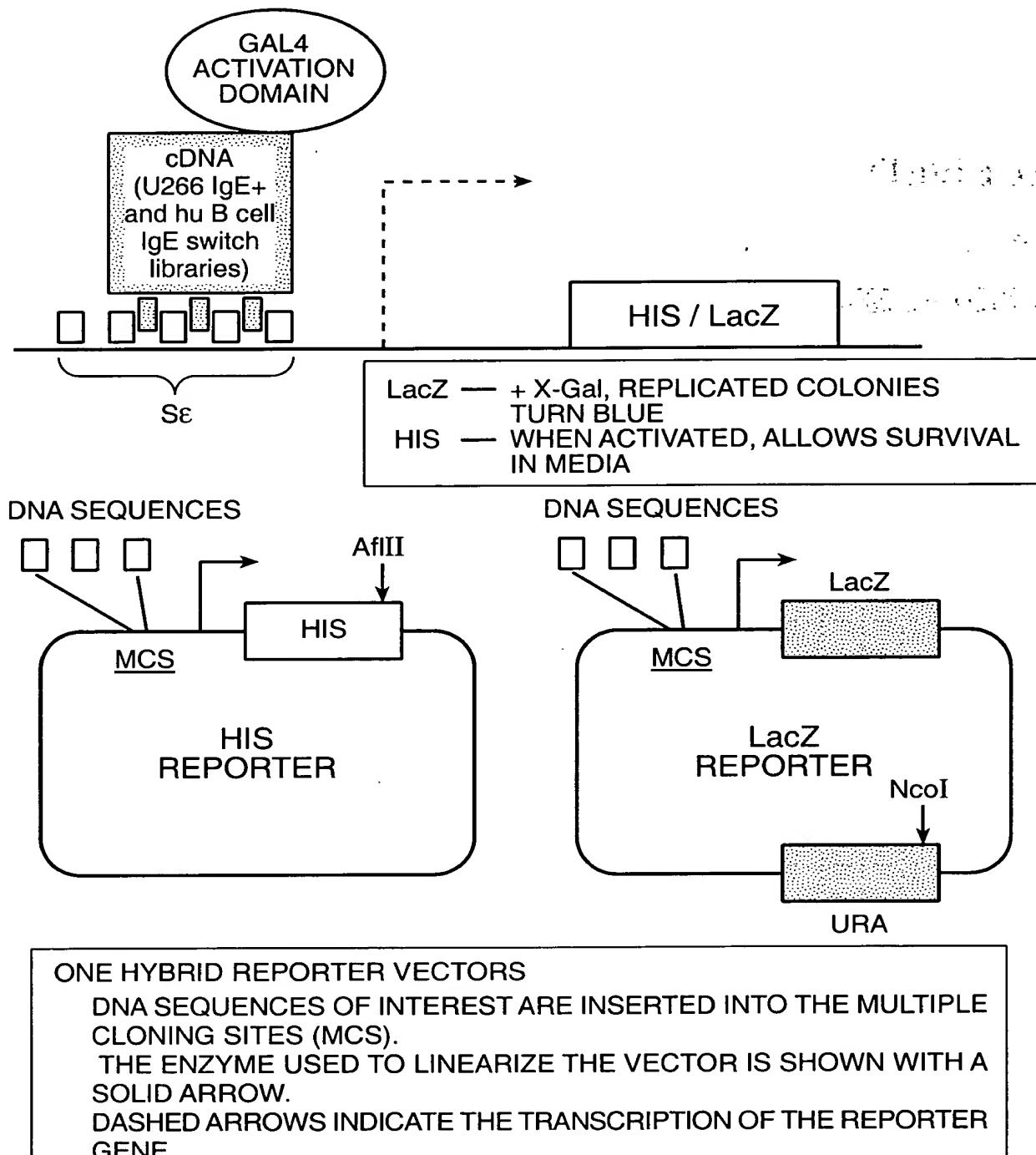


FIG. 2A

HIGHLEDGED AREAS: TARGET SEQUENCES USED IN THE ONE-HYBRID SCREEN  
APPENDIX E

+

## YEAST ONE-HYBRID SCREENING



APPENDIX F

**FIG.\_3**

IL-4 INDUCTION OF GERMLINE  $\epsilon$  mRNA IN THE  
IgM + B CELL LINES: CA-46, MC-116 AND DND39

DND39 + IL-4

DND39 - IL-4

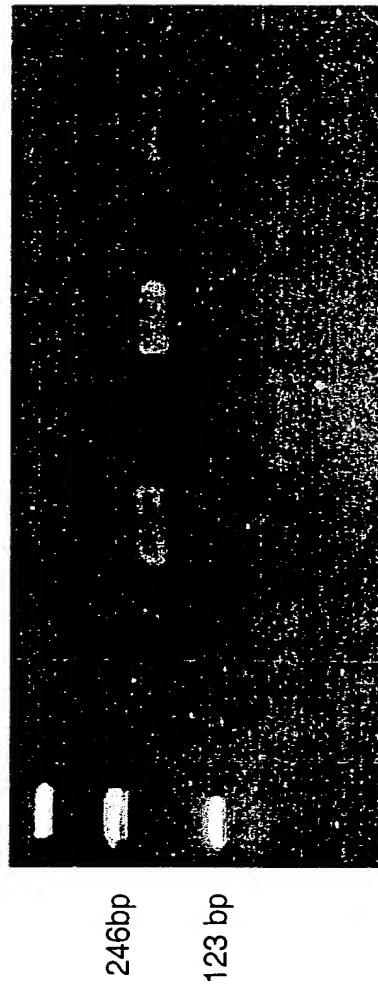
MC-116 + IL-4

MC-116 - IL-4

CA-46 + IL-4

CA-46 - IL-4

NEG. CONT.

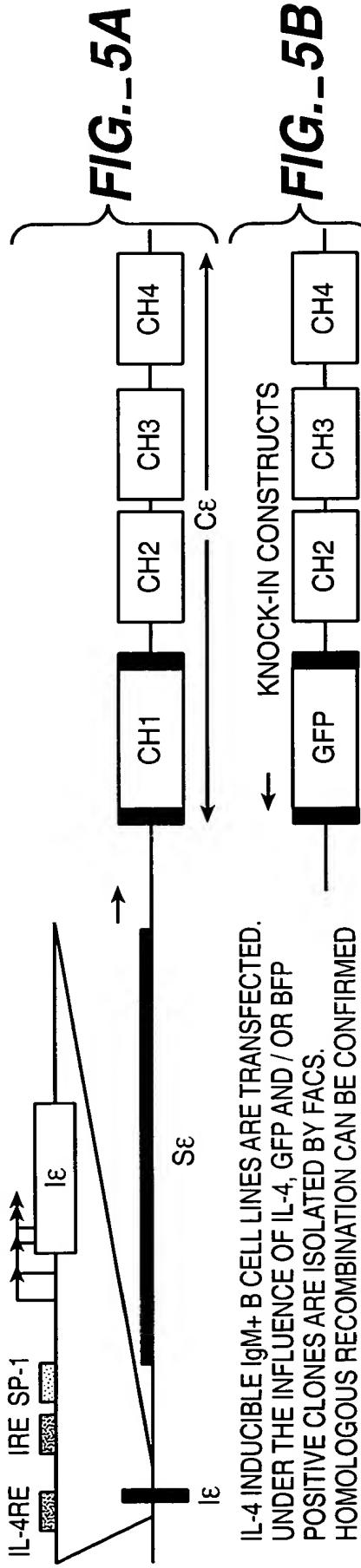


CELLS WERE INCUBATED FOR 48 HRS. IN 300 U / ml OF h-IL-4.

RT-PCR WAS PERFORMED USING PRIMERS SPECIFIC FOR THE GERMLINE  $\epsilon$  EXON AND THE 5'-END OF THE C $\epsilon$  CH1 EXON (PREDICTED SIZE ~ 200 bp).

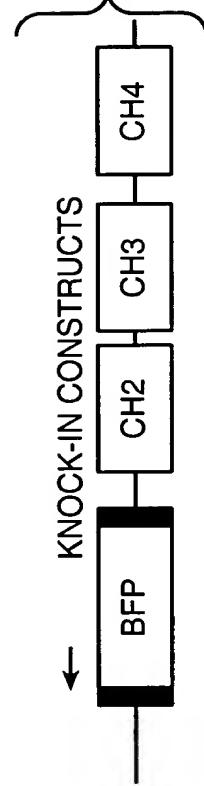
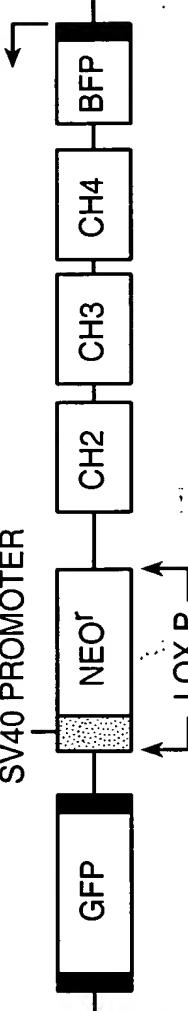
APPENDIX G

FIG.\_4

APPROACHES TO GENERATE GERMLINE  $\epsilon$  PROMOTER KNOCK-IN REPORTER CELL LINES

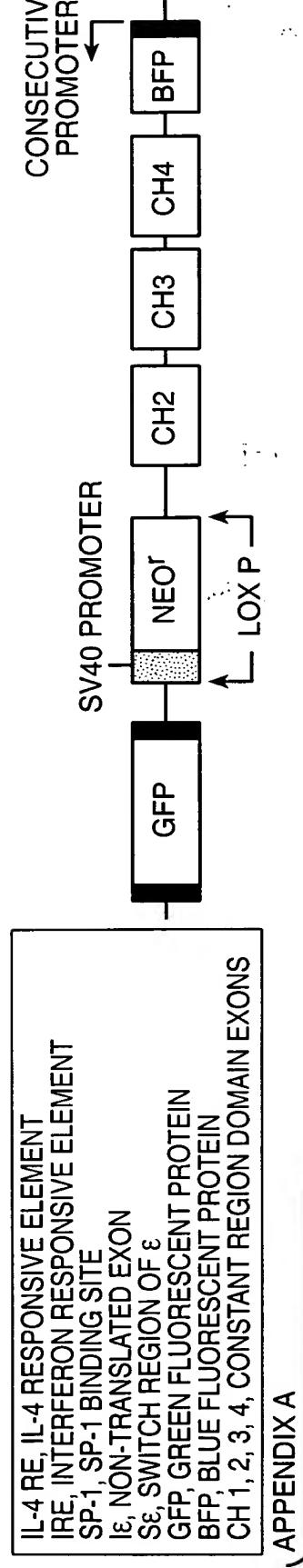
IL-4 INDUCIBLE IgM+ B CELL LINES ARE TRANSFECTED.  
UNDER THE INFLUENCE OF IL-4, GFP AND / OR BFP  
POSITIVE CLONES ARE ISOLATED BY FACS.  
HOMOLOGOUS RECOMBINATION CAN BE CONFIRMED  
BY PCR AND/OR SOUTHERN BLOTH HYBRIDIZATION.

IL-4 INDUCIBLE, IgM+ B CELL LINES ARE TRANSFECTED  
AND SELECTED WITH G418. SURVIVORS ARE SORTED  
FOR THE LACK OF 3' BFP EXPRESSION (DELETED  
DURING HOMOLOGOUS RECOMBINATION). RT-PCR IS  
PERFORMED TO CONFIRM HOMOLOGOUS  
RECOMBINATION. THOSE CLONES ARE TRANSFECTED  
WITH *cre* TO REMOVE THE NEOMYCIN RESISTANCE  
GENE.

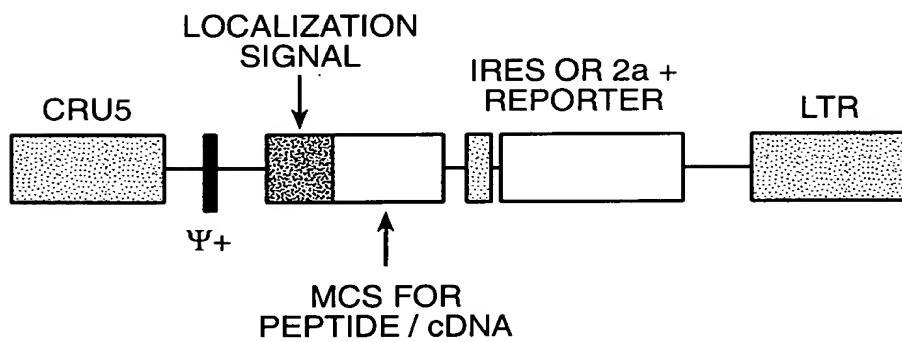
**FIG. 5B**CONSECUTIVE  
PROMOTER

IL-4 RESPONSIVE ELEMENT  
IRE, INTERFERON RESPONSIVE ELEMENT  
SP-1, SP-1 BINDING SITE  
I $\epsilon$ , NON-TRANSLATED EXON  
S $\epsilon$ , SWITCH REGION OF  $\epsilon$   
GFP, GREEN FLUORESCENT PROTEIN  
BFP, BLUE FLUORESCENT PROTEIN  
CH 1, 2, 3, 4, CONSTANT REGION DOMAIN EXONS

APPENDIX A

**FIG. 5D**

## RIGEL BASE VECTOR



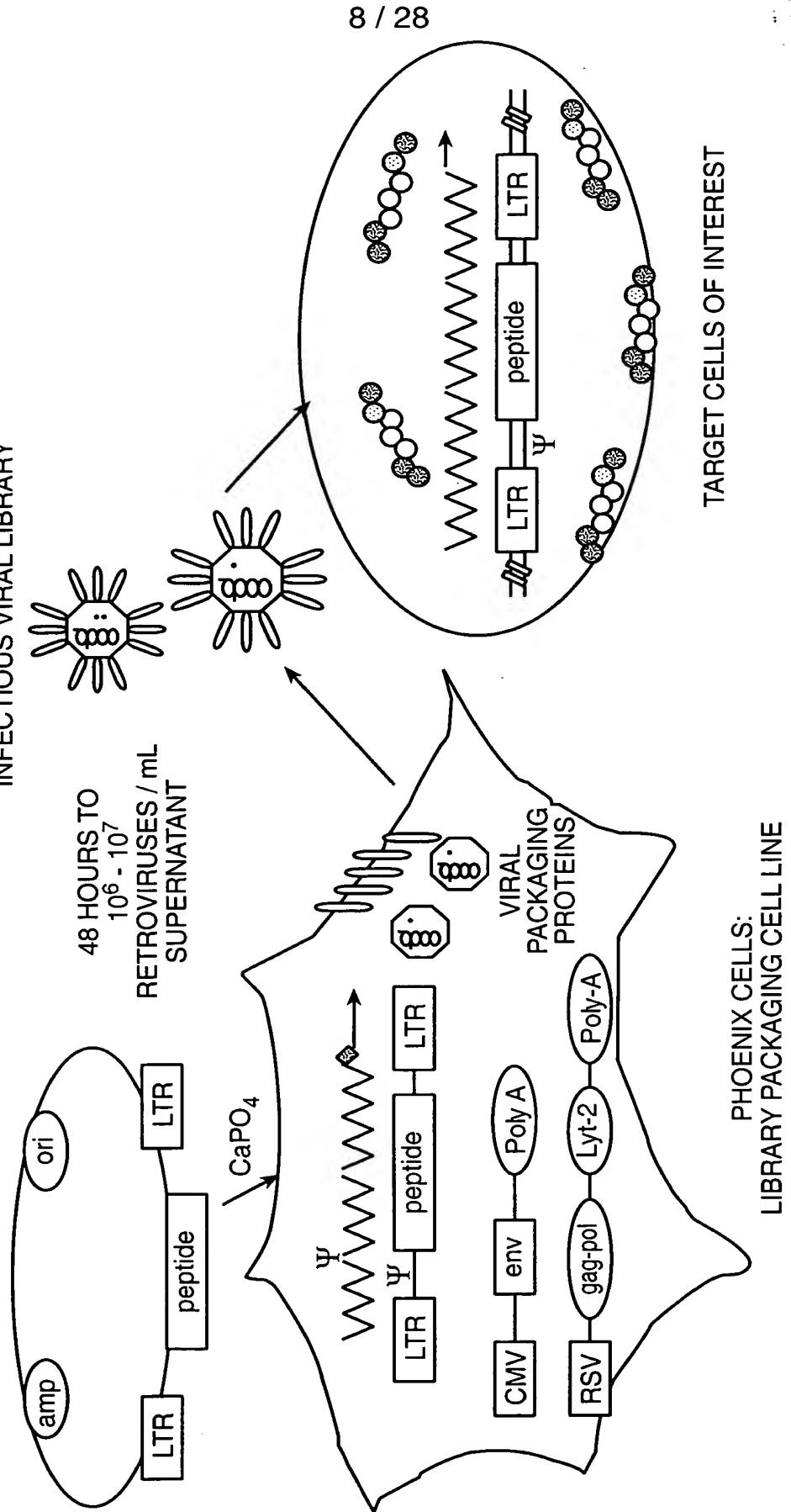
ALL COMPONENTS ARE UNIQUELY CASSETTED FOR FLEXIBILITY

CRU5, MODIFIED LTR  
LTR, LONG TERMINAL REPEAT  
 $\Psi+$ , PACKING SIGNAL  
LOCALIZATION SIGNAL: NUCLEAR, CELL MEMBRANE, GRANULAR  
MCS, MULTIPLE CLONING SITE  
IRES, INTERNAL RIBOSOME ENTRY SITE  
2a, SELF-CLEAVING PEPTIDE

APPENDIX I

***FIG.\_6***

## PROTOCOL FOR TRANSFECTION OF PHOENIX CELLS AND INFECTION OF NONADHERENT TARGET CELLS

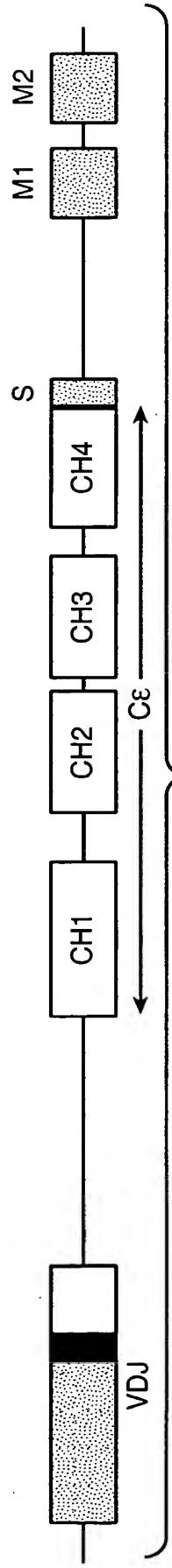


**PHOENIX CELLS:  
LIBRARY PACKAGING CELL LINE**

## APPENDIX I

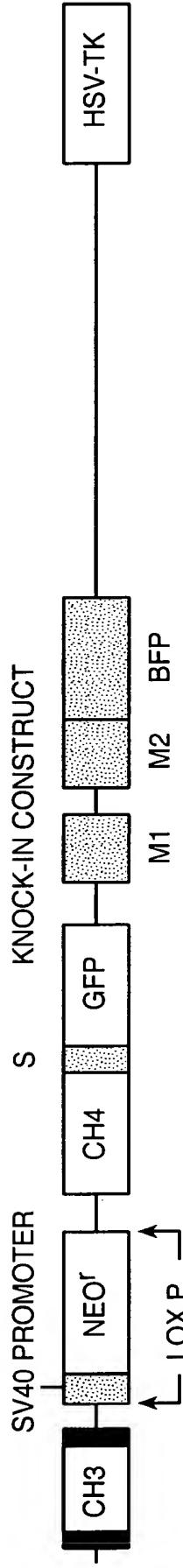
FIG. 7

ε HEAVY CHAIN GFP / BFP KNOCK-IN CELL LINE  
U266 ε HEAVY CHAIN



**FIG..-8A**

S KNOCK-IN CONSTRUCT



U266 CELLS ARE TRANSFECTED AND SELECTED WITH G418. SURVIVORS ARE TREATED WITH GANCICLOVIR (HSV-TK DELETED DURING HOMOLOGOUS RECOMBINATION). RT-PCR IS PERFORMED TO CONFIRM HOMOLOGOUS RECOMBINATION. THOSE CLONES ARE TRANSFECTED WITH *cre* TO REMOVE THE SV40 NEOMYCIN RESISTANCE GENE.

APPENDIX D

**S**, SECRETORY EXON  
**GFP**, GREEN FLUORESCENT PROTEIN  
**BFP**, BLUE FLUORESCENT PROTEIN  
**Neo'**, NEOMYCIN RESISTANCE GENE  
**VDJ**, V REGION EXON  
**CH** 1, 2, 3, 4, CONSTANT REGION DOMAIN EXONS  
**M** 1, M 2, MEMBRANE EXONS  
**HSV-TK**, HERPES SIMPLEX VIRUS-THYMIDINE KINASE

**FIG..-8B**

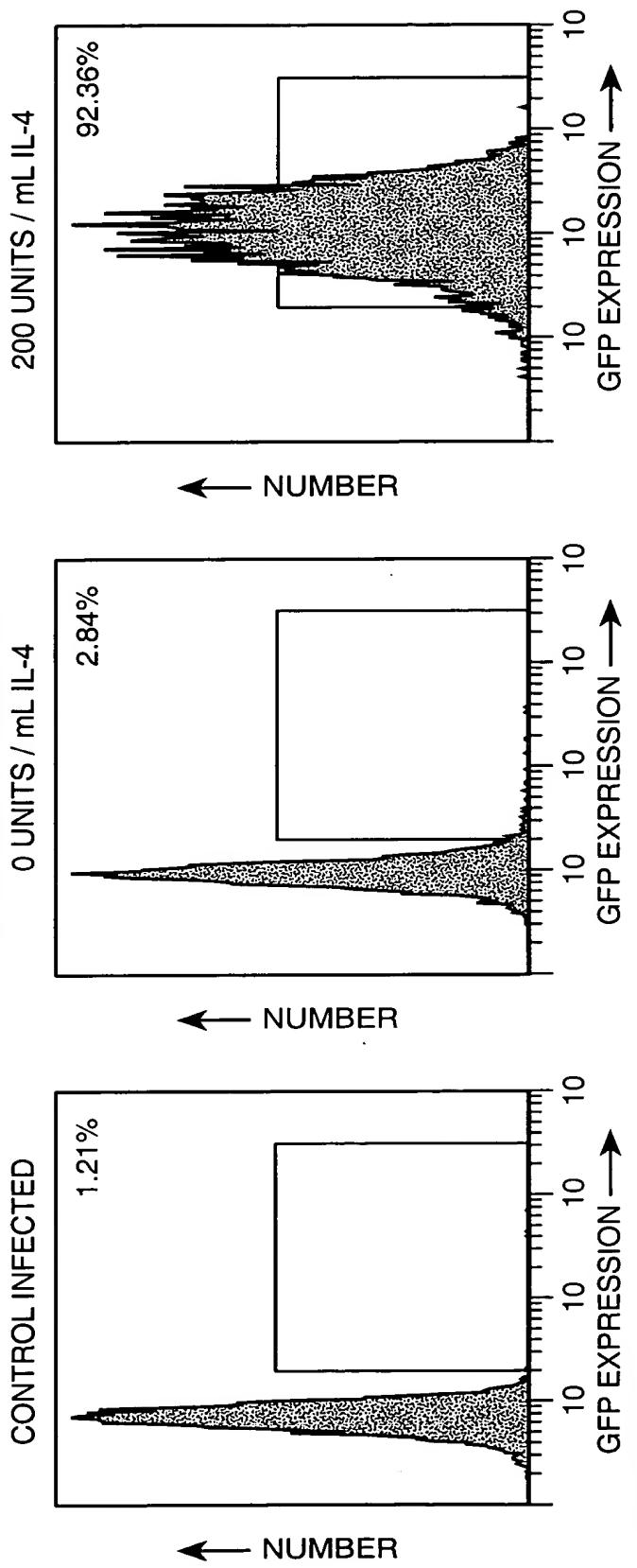
IL-4 INDUCIBLE & PROMOTER REPORTER CELL LINE

REPORTER CONSTRUCT



A-66038-4

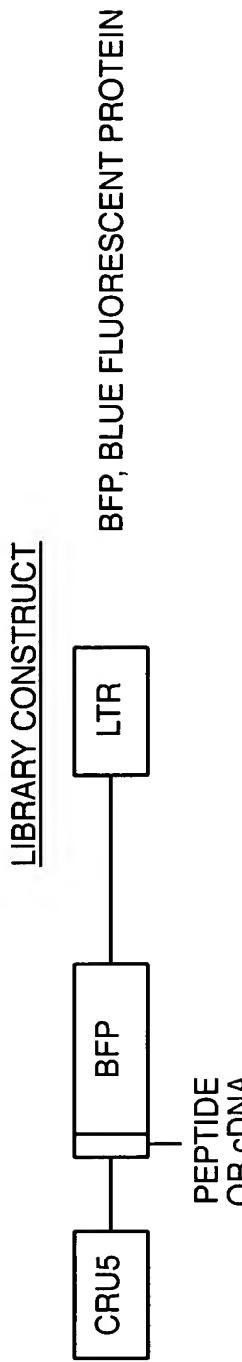
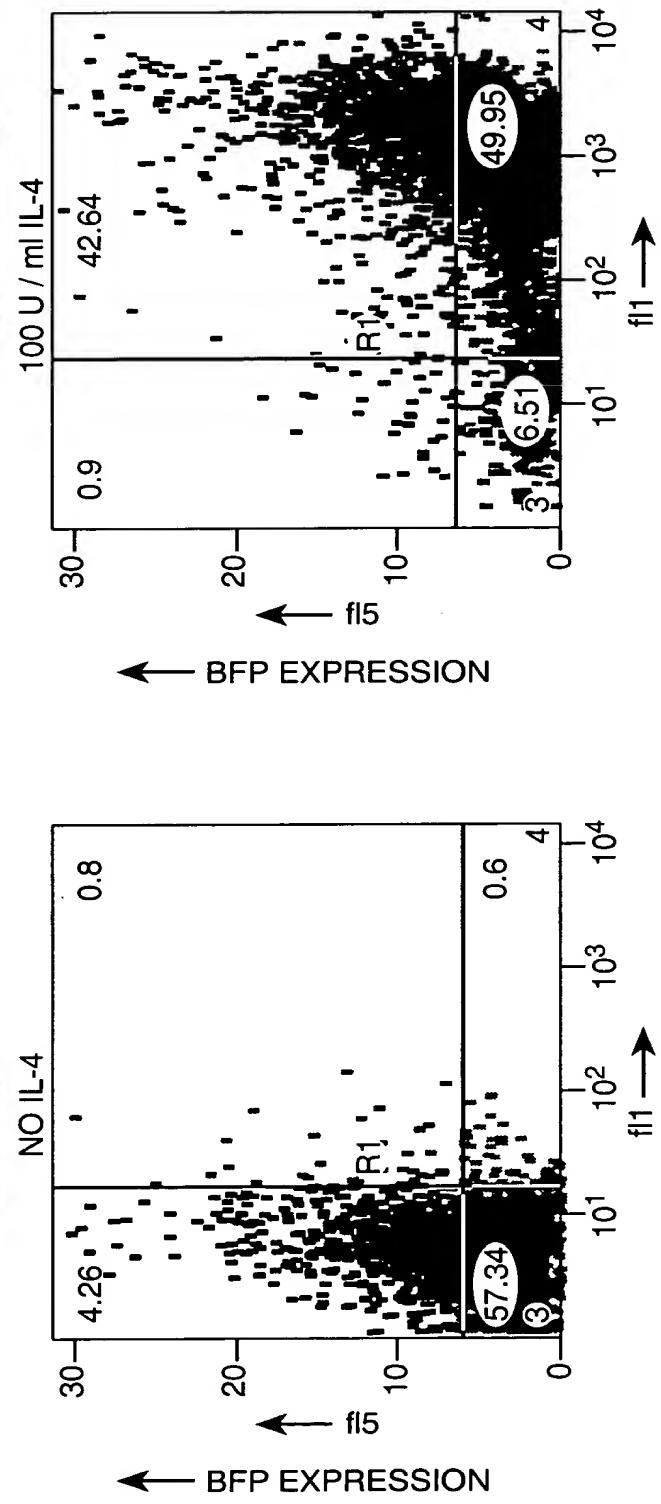
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APPENDIX C

**FIG. 9A**

## REPORTER LINE INFECTED WITH BFP CONSTRUCT

FACS PROFILE OF CELLS WITH BOTH REPORTER AND PEPTIDE LIBRARY

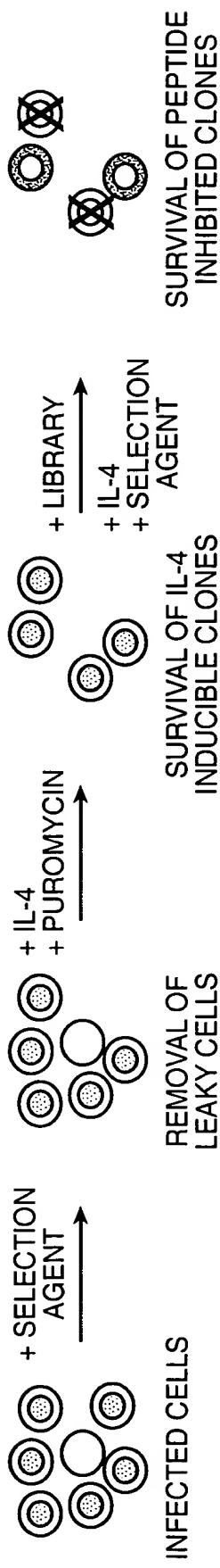
APPENDIX C

GFP EXPRESSION →

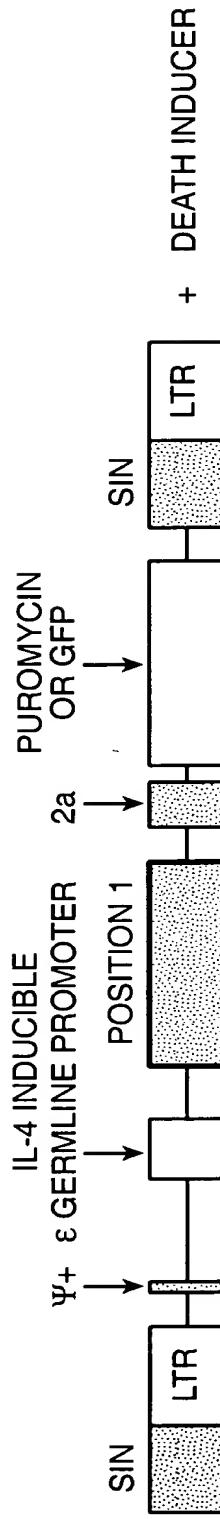
GFP EXPRESSION →

**FIG. 9B**

## SCREEN FOR PEPTIDE INHIBITORS OF THE GERMLINE &amp; PROMOTER



## SURVIVAL CONSTRUCT



## POSITION 1

FAS CHIMERIC RECEPTOR\*

\*(MOUSE FAS/CD8 EXTERNAL + HUMAN TRANSMEMBRANE AND CYTOPLASMIC DOMAINS)

SIN, SELF-INACTIVATING LTR  
LTR, LONG TERMINAL REPEAT

HSV-TK  
P450 2B1  
p21 PEPTIDE

ALL COMPONENTS ARE CASSETTED FOR FLEXIBILITY

GANCICLOVIR  
CYCLOPHOSPHAMIDE

NONE (SELF SELECTION)

APPENDIX D

**FIG. 10**

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1-845 CMV promoter/R/U5 5' LTR  
 1322 GAG ATG-ATC mutation  
 850-2100 extended Ψ region  
 2146-2173 two BstX1 peptide cloning sites  
 2205-2723 ECMV IRES (cloned as EcoR1/Msc1 fragment from  
     pCITE-4a [Novagen])  
 2746-3465 GFP coding region  
 3522-4115 3' LTR  
 4122-6210 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTCGTCTCAAGAACAGCTTGCTCTAGGAGTTCTAATACATCC  
 CAAACTCAAATATATAAAGCATTGACTTGTCTATGCCCTAGTTATTAAATAGTAATCAA  
 TTACGGGGTCATTAGTCATAGCCCATAATGGAGTTCCGCGTTACATAACTACGGTAA  
 ATGGCCCGCCTGGCTGACCGCCAACGACCCCCGCCATTGACGTCAATAATGACGTATG  
 TTCCCATAGTAACGCCAATAGGGACTTCCATTGACGTCAATGGGTGGAGTATTACGGT  
 AAACTGCCACCTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCTATTGACG  
 TCAATGACGGTAAATGGCCGCCCTGGCATTATGCCAGTACATGACCTTATGGGACTTTC  
 CTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTATGCGGTTTGGC  
 AGTACATCAATGGCGTGGATAGCGGTTGACTCACGGGATTCCAAGTCTCCACCCCA  
 TTGACGTCAATGGAGTTGGCACC AAAATCAACGGACTTCCAAAATGTCGTA  
 ACAACTCCGCCATTGACGAAATGGCGGTAGGCATGTACGGTGGGAGGTCTATATAA  
 GCAGAGCTCAATAAAAGAGCCCACAACCCCTACTCGGGCGCAGTCCTCCGATTGACT  
 GAGTCGCCCGGGTACCGTGTATCCAATAACCCCTTGCAGTGCATCCGACTTGTGGT  
 CTCGCTGTTCTGGAGGGTCTCCTCTGAGTGTGACTACCCGTCAAGCGGGGGTCTTT  
 CATTGGGGCTCGTCCGGATCGGAGACCCCTGCCAGGGACCACCGACCCACCC  
 GGAGGTAAGCTGCCAGCAACTATCTGTGTCTGTCCGATTGCTAGTGTCTATGACTGA  
 TTTTATGCGCTCGTCGGTACTAGTTAGCTAACTAGCTCTGTATCTGGCGGACCCGTGG  
 TGGAACTGACGAGTTCGGAACACCCGGCGAACCCCTGGAGACGTCCCAGGGACTTCGG  
 GGGCCGTTTGTGGCCGACCTGAGTCCAAAATCCGATCGTTTGACTCTTGGT  
 CACCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGACGAGAACCTAAAACAGTTCC  
 CGCCTCCGTCTGAATTGGCTTCTGGTTGGGACCGAAGCCGCGCGCGTCTGTCT  
 GCTGCAGCATCGTTCTGTGTCTGTACTGTGTTCTGTGACTGTGTTCTGTATTGTCTGAAAATA  
 TCGGCCCCGGGCCAGACTGTTACCACTCCCTTAAGTTGACCTTAGGTCACTGGAAAGATG  
 TCGAGCGGATCGCTACAACCAGTCGGTAGATGTCAAGAAGAGACGTTGGGTTACCTTCT  
 GCTCTGCAGAATGGCAACCTTAACGTGGATGGCCGCGAGACGGCACCTTAACCGAG  
 ACCTCATCACCCAGGTTAAGATCAAGGTCTTACCTGGCCGATGGACACCCAGACC  
 AGGTCCCCTACATCGTGACCTGGGAAGCCTGGCTTTGACCCCCCTCCCTGGGTCAAGC  
 CCTTTGTACACCCCTAACGCTCCGCCCTCTCTCCATCCGCCCGTCTCTCCCCCTTG  
 AACCTCCTCGTTGACCCGCCCTCGATCCTCCCTTATCCAGCCCTACTCCTCTAG  
 GCGCCCCCATATGCCATATGAGATCTTATATGGGGACCCCCGCCCTGTAAACTTCC  
 CTGACCCCTGACATGACAAGAGTTACTAACAGCCCTCTCCAAAGCTCACTTACAGGCTC  
 TCTACTTAGTCCAGCACGAAGTCTGGAGACCTCTGGCGGCAGCCTACCAAGAACAACTGG  
 ACCGACCGGTGGTACCTCACCCCTTACCGAGTCGGCGACACAGTGTGGTCCGCCGACACC  
 AGACTAAGAACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCTGTGACCAACCCCA  
 CGGCCCTCAAAGTAGACGGCATCGCGCTGGATACACGCCGCCACGTGAAGGCTGCCGA  
 CCCCGGGGGTGGACCATCCTCTAGACTGCCGGATCTCGAGGGATCCACCAACCATGGACCC  
 CCATTAAATTGGAATTCCCTGAGCCCGGGGATCCACTAGTTCTAGAGCGAATTAAATTCC

**FIG.\_11A-1**

GGTTATTTCCACCATATTGCCGTCTTGGCAATGTGAGGGCCGGAAACCTGGCCCTG  
 TCTTCCTGACGAGCATTCTAGGGCTTCCCTCTGCCAAAGGAATGCAAGGTCTGT  
 TGAATGTCGTGAAGGAAGCAGTCCTCTGGAAAGCTCTGAAGACAAACAAACGTCTGTAG  
 CGACCCTTGCAGGCAGCGGAACCCCCCACCTGGCGACAGGTGCCTCTGCCGGCAAAAGC  
 CACGTGTATAAGATAACACCTGCAAAGGCCACAACCCAGTGCCACGTTGTGAGTTGGA  
 TAGTTGTGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTCAACAAGGGCTGAAGGATG  
 CCCAGAAGGTACCCATTGTATGGATCTGATCTGGGCCTCGGTGCACATGCTTACAT  
 GTGTTAGTCGAGGTTAAAAAACGTCTAGGCCCGAACACGGGACGTGGTTTCCT  
 TTGAAAAACACGATGATAATATGGGGATCCACCGGTGCCACCATGGTGAGCAAGGGCG  
 AGGAGCTGTTCACCGGGTGGTGCCTCGAGCTGGACGGCACGTAACGGCC  
 ACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCCTGA  
 AGTTCATCTGCACCAACCGCAAGCTGCCGTGCCCTGCCACCGTGCACCCCTGA  
 CCTACGGCGTCAGTCTCAGCGCTACCCGACCACATGAAGCAGCACGACTTCTCA  
 AGTCCGCCATGCCGAAGGCTACGTCCAGGAGCGCACCATCTTCAAGGACGACGGCA  
 ACTACAAGACCCGCGCGAGGTGAAGTTCGAGGGCGACACCCCTGGTAACCGCATCGAGC  
 TGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACA  
 ACAACAGCCACAACGTCTATATCATGGCGACAAGCAGAAGAACGGCATCAAGGTGA  
 TCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTGCCGACCAACTACAGCAGA  
 ACACCCCATCGCGACGGCCCGTGTGCTGCCGACAACCAACTACCTGAGCACCCAGT  
 CCGCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGCCTGCTGGAGTCTG  
 CCGCCGCCGGGATCACTCTCGCATGGACGAGCTGTACAAGTAAAGCGGCCGCTCGACGA  
 TAAAATAAAAGATTTATTTAGTCTCCAGAAAAAGGGGAAATGAAAGACCCACCTGTA  
 GGTTGGCAAGCTAGCTTAAGTAACGCCATTTGCAAGGCATGGAAAAATACATACTGA  
 GAATAGAGAAGTCAGATCAAGGTAGGAACAGATGGAACAGCTGAATATGGGCCAAACA  
 GGATATCTGGTAAGCAGTCCTGCCCGGCTCAGGGCAAGAACAGATGGAACAGCTG  
 AATATGGGCCAAACAGGATATCTGTGGTAAGCAGTCCTGCCCGGCTCAGGGCAAGAA  
 CAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTCTAGAGAACCATCAGATGTT  
 CAGGGTCCCCAAGGACCTGAAATGACCCGTGCTTATTTGAACTAACCAATCAGTT  
 CTTCTCGCTTCTGTCGCGCTTCTGCTCCCGAGCTCAATAAGAGCCCACAACCC  
 TCACTCGGGCGCCAGTCCTCCGATTGACTGAGTCGCCGGTACCGTGTATCCAATAA  
 ACCCTCTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCTGGGAGGGTCTCTG  
 GTGATTGACTACCGTCAGCGGGGTCTTCATTCCGACTTGTGGTCTCGCTGCTTGG  
 GAGGGTCTCCTCTGAGTGATTGACTACCGTCAGCGGGGTCTCACATGCAGCATGTAT  
 CAAAATAATTGGTTTTCTTAAGTATTACATAAATGCCATAGTTGCATTAAAT  
 GAATCGGCCAACCGCGGGGAGAGGCGGTTGCGTATTGGCGCTTCCGCTTCCGCT  
 CACTGACTCGCTCGCTCGGTGTTGGCTGCGAGCGGTATCAGCTCACTCAAAGGC  
 GGTAAACGGTTATCCACAGAATCAGGGATAACGCAGGAAAGAACATGTGAGCAAAAGG  
 CCAGCAAAAGGCCAGGAACCGTAAAAGGCCGCGTGGCTGGCGTTTCCATAGGCTCCG  
 CCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGG  
 ACTATAAAAGATACCAAGGCCTTCCCCCTGGAAGCTCCCTCGTGCCTCTGTTCCGAC  
 CCTGCCGCTTACCGGATACCTGTCCGCTTCTCCCTCGGGAAAGCGTGGCGCTTCTCA  
 TAGCTCAGCGCTGTAGGTATCTCAGTTGGTGTAGGTGCTGCCAGCTGGCTGTGT  
 GCACGAACCCCCGGTTCAAGCCGACCGCTGCCCTATCCGGTAACATCGTCTTGAGTC  
 CAACCCGGTAAGACACGACTTATGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG  
 AGCGAGGTATGTAGGCAGGTGCTACAGAGTTCTGAAGTGGTGGCCTAACTACGGCTACAC

TAGAAGGACAGTATTGGTATCTGCCTCTGCTGAAGCCAGTTACCTCGGAAAAAGAGT  
TGGTAGCTCTTGATCCGGCAAAACAAACCCACCGCTGGTAGCGGTGGTTTTGTTGCAA  
GCAGCAGATTACCGCAGAAAAAGGATCTAAGAAGATCCTTGATCTTCTACGGG  
GTCTGACGCTCAGTGGAACGAAAACACGTTAAGGGATTTGGTCATGAGATTATCAA  
AAGGATCTTCACCTAGATCCTTAAATTAAAATGAAGTTGCGCAAATCAATCTAAAG  
TATATATGAGTAAACTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTC  
AGCGATCTGCTATTCGTTCATCCATAGTTGCCTGACTCCCCGTGTTAGATAACTAC  
GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATAACCGCGAGACCCACGCTC  
ACCGGCTCCAGATTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGG  
TCCTGCAACTTATCCGCCTCCATCCAGTCTATTAAATTGTTGCCATTGCTACAGGCATGTTGTC  
TAGTTGCCAGTTAATAGTTGCGAACGTTGCTACAGGCATGTTGTC  
ACGCTCGTCGTTGGTATGGCTTCATTCACTCCGGTCCAACGATCAAGGCAGATTAC  
ATGATCCCCATGTTGCAAAAAGCGGTTAGCTCCTCGGTCCGATGTTGTCAG  
AAGTAAGTTGCCCGCAGTGTATCACTCATGGTTATGGCAGCAGTGCATAATTCTCTTAC  
TGTCAATGCCATCCGTAAGATGCTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTG  
AGAATAGTGTATGCGCGACCGAGTTGCTCTTGGCAACACGGGATAATACCGC  
GCCACATAGCAGAACTTAAAGTGCCTCATATTGGAAAACGTTCTCGGGCGAAAACCT  
CTCAAGGATCTACCGCTGTTGAGATCAGTCAGTTGATGTAACCCACTCGTGCACCCAACTG  
ATCTTCAGCATCTTACTTCAACCAGCGTTCTGGGTGAGCAAAAACAGGAAGGCAAAA  
TGCCGCAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATAACTCATACTCTTCTTT  
TCAATATTATTGAAGCATTATCAGGGTTATTGTCATGAGCGGATAACATATTGAATG  
TATTTAGAAAAATAACAAATAGGGTCCCGCAGATTTC

**FIG.\_ 11A-3**

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1-845 CMVpromoter/R/U5 5' LTR  
 1322 GAG ATG-ATC mutation  
 850-2100 extended ψ r gion  
 2151-2865 GFP coding region  
 2866-2894 GGGSGGG linker  
 2895-2952 FMDV 2a cleavage sequence  
 2953-3004 BstX1/BstX1/HinD3/Hpa1/Sal1/Not1 polylinker  
 3052-3645 3' LTR  
 3652-5715 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTCGTCTCAAGAACAGCTTGCTTAGGAGTTCTAATACATC  
 CCAAACCTAAATATATAAAGCATTGACTTGTCTATGCCCTAGTTATTAATAGTAATC  
 AATTACGGGGTCATTAGTCATAGCCCATAATGGAGTTCCGGTACATAACTACGG  
 TAAATGGCCCGCCTGGCTGACCGCCAAACGACCCCCGCCATTGACGTCAATAATGACG  
 TATGTTCCCATACTAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTT  
 ACGGTAACACTGCCACTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCTA  
 TTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCAGTACATGACCTTATGG  
 GACTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTATGCG  
 GTTTGGCAGTACATCAATGGCGTGGATAGCGGTTGACTCACGGGATTCCAAGTC  
 TCCACCCCATTGACGTCAATGGAGTTGGCACCAAAATCAACGGGACTTCCA  
 AAATGTCGTAACAACCTCCGCCATTGACGCAAATGGCGGTAGGCATGTACGGTGGGA  
 GGTCTATATAAGCAGAGCTCAATAAAAGAGGCCACAACCCCTACTCAGGGCGCCAGTC  
 CTCCGATTGACTGAGTCGCCGGTACCGTGTATCCAATAACCCCTTGCAGTTGCA  
 TCCGACTTGTGGTCTCGCTGTTCTGGGAGGGTCTCCTCTGAGTGAATTGACTACCGT  
 CAGCGGGGGCTTCAATTGGGGCTCGCCGGATCGGAGACCCCTGCCAGGGACC  
 ACCGACCCACCACCGGGAGGTAAGCTGCCAGCAACTTATCTGTGTCTGCGATTGTC  
 TAGTGTCTATGACTGATTATGCGCTCGCTGGTACTAGTTAGCTAACTAGCTCTGT  
 ATCTGGCGGACCCGTGGACTGACGAGTTCGAACACCCGGCGAACCTGGGAG  
 ACGTCCCAGGGACTTCGGGGCGTTTGTGGCCGACCTGAGTCAAACCTCCGAT  
 CGTTTGGACTCTTGGTCACCCCTTAGAGGGAGATATGTGGTTCTGGTAGGAGA  
 CGAGAACCTAAACAGTTCCGCCTCCGTCTGAATTGGCTTGGGACCGAA  
 GCCCGCCGCGCGTCTGTCTGCTGCAGCATCGTCTGTGTTCTGTACTGTG  
 TTTCTGTATTGTCTGAAAATATCGGCCGGGCCAGACTGTTACCAACTCCCTTAAGTT  
 GACCTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAAACCTGGTAGATGTCA  
 AGAAGAGACGTTGGTTACCTCTGCTCGAGAATGCCAACCTTAACGTGGATGG  
 CCGCGAGACGGCACCTTAACCGAGACCTCATCACCCAGGTTAGATCAAGGTCTT  
 ACCTGGCCCGCATGGACACCCAGACCGAGGTCCCTACATCGTGACCTGGGAAGCCTT  
 CTTTGACCCCTCCCTGGTCAGGCCCTTGACACCTAACGCTCCGCTCCTCTT  
 CCTCCATCCGCCCGTCTCTCCCTTGAAACCTCCTCGTTGACCCCGCCTCGATCCTC  
 CCTTATCCAGCCCTCACTCCCTCTAGGCGCCCCATATGCCATATGAGATCTT  
 ATGGGGCACCCCGCCCTGTAAACTCCCTGACCCGTACATGACAAGAGTTACTAAC  
 AGCCCTCTCTCCAAGCTCACCTACAGGCTCTACTTAGTCCAGCACGAAGTCTGGAG  
 ACCTCTGGCGGCAGCCTACCAAGAACAACTGGACCGACCGGTGGTACCTCACCCCT  
 GAGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGG  
 AAAGGACCTTACACAGTCCTGCTGACCAACCCCAACGCCCTCAAAGTAGACGGCATCGC  
 AGCTTGGATACACGCCGCCACGTGAAGGCTGCCGACCCGGGGTGGACCACCTCT  
 GACTGCCGGATCTCGAGGGATCCACCATGGTGAGCAAGGGCGAGGAGCTGTT  
 CACCGGG

**FIG.\_ 11B-1**

GTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGCCACAAGTTCAGCGTGTC  
 CGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCCTGAAGTTCATCTGCACCA  
 CGCGCAAGCTGCCGTGCCCTGGCCACCCCTCGTGAACCGACCCCTGACCTACGGCGTGCA  
 TGCTTCAGCCGCTACCCCGACCACATGAAGCAGCAGCAGCTTCAAGTCCGCCATGCC  
 CGAAGGCTACGTCCAGGAGCGCACCATCTTCAAGGACGACGGCAACTACAAGACCC  
 GCGCCGAGGTGAAGTTCGAGGGCGACACCCCTGGTGAACCGCATCGAGCTGAAGGGCATC  
 GACTTCAAGGAGGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACATACAACAGCCA  
 CAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACCTCAAGATCC  
 GCCACAAACATCGAGGACGGCAGCGTGCAGCTGCCGACCACTACCAGCAGAACACCCCC  
 ATCGGGCGACGGCCCCGTGCTGCTGCCGACAACCAACTACCTGAGCACCCAGTCCGCC  
 GAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCTGCTGGAGTTCGTGACCGCCG  
 CGGGGATCACTCTGGCATGGACGAGCTGTACAAGGAATTGGAGGTGGCAGCGTGGC  
 GGTCAAGCTGTTGAATTGACCTTCTAAACTTGCAGGAGACGTCGAGTCCAACCCCTGG  
 GCCCACCACCATGGAAGCTTCAATTGGTTAACGTCGACGCCGCTCGAC  
 GATAAAATAAAAGATTATTTAGTCTCCAGAAAAAGGGGGAAATGAAAGACCCACCT  
 GTAGGTTGGCAAGCTAGCTTAAGTAACGCCATTGCAAGGCATGGAAAATACATAA  
 CTGAGAATAGAGAAGTCAGATCAAGGTCAAGAACAGATGGAACAGCTGAATATGGGCC  
 AACAGGATATCTGTGTAAGCAGTTCTGCCCGCTCAGGGCCAAGAACAGATGGAA  
 CAGCTGAATATGGCCAAACAGGATATCTGTGTAAGCAGTTCTGCCCGCTCAGGG  
 CCAAGAACAGATGGTCCCCAGATGCGGCCAGCCCTCAGCAGTTCTAGAGAACCATCA  
 GATGTTCCAGGGTGCCCAAGGACCTGAAATGACCCCTGTGCCATTGGAACTAACCA  
 ATCAGTTGCTCTCGCTTCTGTTGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGC  
 CCACAAACCCCTCACTCGGGGCGCCAGTCCCTCCGATTGACTGAGTCGCCGGTACCGT  
 GTATCCAATAAAACCTCTGAGTTGACTACCCGTCAAGGGGGTCTTCATTCCAGTTGTGGT  
 GGTCTCCTCTGAGTGATTGACTACCCGTCAAGGGGGTCTTCATTCCAGTTGTGGT  
 CTCGCTGCCATTGGAGGGTCTCTGAGTGATTGACTACCCGTCAAGGGGGTCTTC  
 CATGCAGCATGTATCAAATTGTTTCTTAAGTATTACATTAAATGGC  
 CATAGTTGCATTAATGAATCGCCAACGCGCGGGAGAGGGGGTTCGCTATTGGCGCT  
 CTTCCGCTTCCTCGCTACTGACTCGCTCGCTCGGTCGCTGCCGAGCGGTA  
 TCAGCTCACTCAAAGCGGTAATACGGTTATCCACAGAACGAGCTCGGCTACCG  
 GAACATGTGAGCAAAGGCCAGCAAAGGCCAGGAACCGTAAAAGGCCGCTGGCTGG  
 CGTTTTCCATAGGCTCCGCCCTGACGAGCATCACAAAATCGACGCTCAAGTCAG  
 AGGTGGGAAACCCGACAGGACTATAAGATACCGGTTCCCGCTGGAAAGCTCC  
 CGTGCCTCTCCTGTTCCGACCCCTGCCGTTACCGGATACCTGTCGCCCTTCTCC  
 CGGGAAAGCGTGGCGCTTCTCATAGCTCACGCTGTAGGTATCTCAGTTGGTGTAGG  
 GTTCGCTCCAAGCTGGCTGTGACGAACCCCGTTCAAGCCCAGCGCTGCC  
 ATCCGGTAACTATCGTCTTGAGTCCAACCGGTAAGACACGACTATGCCACTGGCAG  
 CAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGAGGGCTACAGAGTTCTG  
 AAGTGGTGGCTAACTACGGTACACTAGAAGGACAGTATTGGTATCTGCGCTCTGCT  
 GAAGCCAGTTACCTTGGAAAAAGAGTGGTAGCTCTGATCCGGCAAACAAACCC  
 CTGGTAGCGGTGGTTTTGTTGCAAGCAGCAGATTACGCGCAGAAAAAGGATCT  
 CAAGAAGATCCCTTGATCTTCTACGGGTCTGACGCTCAGTGGAAACGAAA  
 TCAAGGGATTTGGTATGAGATTATCAAAAGGATCTCACCTAGATCTTAAATT  
 AAAAATGAAGTTGCGCAAATCAATCTAAAGTATATGAGTAAACTGGTCTGACAGT  
 TACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTGTT  
 AGTTGCCTGACTCCCCGTGTAGATAACTACGATAACGGGAGGGCTTACCATCTGGC  
 CCAGTGCTGCAATGATAACGCGAGACCCACGCTACCGGCTCCAGATTATCAGCAATA

**FIG.\_ 11B-2**

AACCAGCCAGCCGGAAAGGGCCAGCGCAGAAGTGGCCTGCAACTTATCCGCCTCCAT  
CCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTCGCCAGTTAATAGTTGC  
GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTACGCTCGTCGTTGGTATGGCT  
TCATTCAGCTCCGGTTCCCAACGATCAAGGCAGTTACATGATCCCCATGTTGTGCAA  
AAAAGCGGTTAGCTCCTCGGTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGT  
TATCACTCATGGTTATGGCAGCACTGCATAATTCTTACTGTCAATGCCATCCGTAAGA  
TGCTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCG  
ACCGAGTTGCTCTGCCCGGTCAACACGGATAATACCGCGCCACATAGCAGAACTT  
TAAAAGTGCTCATCATGGAAAACGTTCTCGGGCGAAAACCTCTCAAGGATCTTACCG  
CTGTTGAGATCCAGTTGATGTAACCCACTCGTGCACCCAACTGATCTCAGCATCTT  
TACTTCACCAAGCGTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAGG  
GAATAAGGGGACACGGAAATGTTGAATACTCATACTCTTCCTTTCAATATTATTGA  
AGCATTATCAGGGTTATTGTCTCATGACATTAACCTATAAAAATAGGCGT

**FIG.\_ 11B-3**

1-845 CMVpormoter/R/U5 5' LTR  
 1322 GAG ATG-ATC mutation  
 850-2100 extended ψ region  
 2146-2173 two BstX1 peptide cloning sites  
 2173-2214 EcoR1/Apa1/Hpa1/Not1 polylinker  
 2262-2855 3' LTR  
 2855-4901 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTCGTCTCAAGAACAGCTTGCTCTAGGAGTTCTAATACATC  
 CCAAACCTCAAATATATAAAGCATTTGACTTGTCTATGCCCTAGTTATTAAATAGTAATC  
 AATTACGGGGTCATTAGTCATGCCATATATGGAGTTCCGCGTTACATAACTTACGGT  
 AAATGGCCCGCCTGGCTGACCGCCAACGACCCCCGCCATTGACGTCAATAATGACGT  
 ATGTTCCCATACTAACGCCAATAGGGACTTCCATTGACGTCAATGGGTGGAGTATTTA  
 CGGTAAACTGCCCACTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCTAT  
 TGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCAGTACATGACCTTATGGG  
 ACTTTCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTATGCGG  
 TTTTGGCAGTACATCAATGGCGTGGATAGCGGTTGACTCACGGGATTCCAAGTCT  
 CCACCCATTGACGTCAATGGAGTTGGCACCATAACGGACTTCAA  
 AATGTCGTAACAACCTCCGCCCCATTGACGCAAATGGCGGTAGGCATGTACGGTGGGAG  
 GTCTATATAAGCAGAGCTCAATAAAAGAGCCCACAACCCCTACTCGGGCGCCAGTCC  
 TCCGATTGACTGAGTCGCCGGGTACCCGTATCCAATAACCCCTTGCAGTTGCAT  
 CCGACTTGTGGTCTCGCTGTTCTGGGAGGGTCTCTTGAGTGATTGACTACCCGTC  
 AGCGGGGGTCTTCATTGGGGCTCGCCGGATCGGAGACCCCTGCCAGGGACCA  
 CCGACCCACCACCGGGAGGTAAGCTGCCAGCAACTTATCTGTGTCTGTCCGATTGTCT  
 AGTGTCTATGACTGATTATGCGCTCGCTGGTACTAGTTAGCTAACTAGCTCTGTA  
 TCTGGCGGACCGTGGTGGAACTGACGAGTTCGGAACACCCGGCGAACCCCTGGGAGA  
 CGTCCCAGGGACTTCGGGGCCGTTTGTGGCCGACCTGAGTCCAAAATCCGATC  
 GTTTGGACTCTTGGTCACCCCTAGAGGAGGGATATGTGGTTCTGGTAGGAGAC  
 GAGAACCTAAAACAGTCCGCCCTCGTAATTGGCTTGGTTGGGACCGAAG  
 CGCGCCGCGCGTCTGTCTGCTGCAGCATGTTCTGTCTGTCTGACTGTGT  
 TTCTGTATTGTCTGAAAATATCGGCCGGCAGACTGTTACCAACTCCCTTAAGTTG  
 ACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTACAACCAAGTCGGTAGATGTC  
 GAAGAGACGTTGGTTACCTCTGCTCTGAGAATGGCAACCTTAACGTCGGATGGC  
 CGCGAGACGGCACCTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTCA  
 CCTGGCCCGCATGGACACCCAGACCAGGTCCCTACATCGTGACCTGGGAAGCCTTGGC  
 TTTGACCCCTCCCTGGGTCAAGCCCTTGTACACCTAAGCTCCGCTCCTCTTC  
 CTCCATCCGCCCGTCTCTCCCCCTTGAACCTCCTCGTTGACCCCGCCTCGATCCTCC  
 CTTTATCCAGCCCTCACTCCTCTAGGCGCCCCATATGCCATATGAGATCTTATA  
 TGGGGCACCCCGCCCTGTAAACTCCCTGACCTGACATGACAAGAGTTACTAAC  
 GCCCCTCTCCAAGCTCACTTACAGGCTCTACTTAGTCCAGCACGAAGTCTGGAGA  
 CCTCTGGCGGCAGCCTACCAAGAACACTGGACCGACCCGGTGGTACCTACCCCTACCG  
 AGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGG  
 AAGGACCTTACACAGTCTGCTGACCAACCCACCGCCCTAAAGTAGACGGCATCGCA  
 GCTTGGATAACGCCGCCACGTGAAGGCTGCCGACCCGGGGTGGACCACCTCTAG  
 ACTGCCGGATCTCGAGGGATCCACCAACCATGGACCCCATTAATTGGAATTCGGGGCC  
 CAAGCTTGTAAACGTCGACGCCGCCGTCGACGATAAAATAAAGATTTATTAG  
 TCTCCAGAAAAGGGGGAAATGAAAGACCCCACCTGTAGGTTGGCAAGCTAGCTTAAG  
 TAACGCCATTGCAAGGCATGGAAAAATACATAACTGAGAATAGAGAAGTTCAGATCA

**FIG.\_ 11C-1**

AGGTCAAGAACAGATGGAACAGCTGAATATGGGCCAACAGGATATCTGTGGTAAGCAG  
 TTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTGAATATGGGCCAACAGGA  
 TATCTGTGGTAAGCAGTTCTGCCCCGGCTCAGGGCCAAGAACAGATGGTCCCCAGATG  
 CGGTCCAGCCCTCAGCAGTTCTAGAGAACCATCAGATGTTCCAGGGTCCCCAAGGA  
 CCTGAAATGACCTGTGCCTTATTGAACTAACCAATCAGTCGCTCTCGCTCTGTT  
 CGCGCCTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCCTCACTGGGGCGCC  
 AGTCCCTCGATTGACTGAGTCGCCGGTACCCGTATCCAATAAACCCCTTGCAGT  
 TGCATCCGACTTGTGGTCTCGCTGTTCTGGGAGGGTCTCCTGTGAGTGATTGACTAC  
 CCGTCAGCGGGGTCTTCATTCGACTTGTGGTCTCGCTGCCCTGGGAGGGTCTCCT  
 CTGAGTGATTGACTACCCGTCAAGCGGGGTCTTCACATGCAGCATGTATCAAATTAAAT  
 TTGGTTTTTTCTTAAGTATTACATTAAATGGCCATAGTTGCATTAATGAATCGGCC  
 AACGCGCGGGGAGAGGCAGTTCGCTATTGGCGCTTCCGCTTCGCTCACTGACT  
 CGCTGCGCTCGGTCTGGCTGCGGAGCGGTATCAGCTCACTCAAAGCGGTAAATA  
 CGGTTATCCACAGAACATCAGGGATAACGCAGGAAAGAACATGTGAGCAAAGGCCAGCA  
 AAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCTTTCCATAGGCTCCGCCCC  
 CTGACGGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTA  
 TAAAGATAACCAAGCGTTCCCCCTGGAAGCTCCCTCGCGCTCTCCTGTTCCGACCC  
 GCCGCTTACCGGATACCTGTCCGCTTCTCCCTCGGAAGCGTGGCGCTTCTCATA  
 GCTCACGCTGTAGGTATCTCAGTTGGTGTAGGTCTCGCTCCAAGCTGGCTGTG  
 CACGAACCCCCCGTTAGCCGACCGCTGCGCCTTATCCGGTAACATACGTCTTGAGTC  
 CAACCCGGTAAGACACGACTTATGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCA  
 GAGCGAGGTATGTAGGGGTGCTACAGAGTTCTGAAGTGTTGGCTTAACACTACGGCTAC  
 ACTAGAAGGACAGTATTGGTATCTCGCTCTGCTGAAGGCCAGTTACCTTCGGAAAAAG  
 AGTTGGTAGCTTGTATCCGGAAACAAACCACCGCTGGTAGCGGTGGTTTTTTGTT  
 GCAAGCAGCAGATTACCGCAGAAAAAAAGGATCTCAAGAAGATCCTTGATTTCT  
 ACGGGTCTGACGCTCAGTGGAACGAAACTCACGTTAAGGGATTTGGTATGAGATT  
 ATCAAAAAGGATCTCACCTAGATCCTTAAATTAAAAATGAAGTTGCGCAAATCAA  
 TCTAAAGTATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCA  
 CCTATCTCAGCGATCTGTCTTTGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTA  
 GATAACTACGATAACGGGAGGGCTTACCATCTGGCCCCAGTGTGCAATGATACCGCGAG  
 ACCCACGCTCACCGGCTCCAGATTATCAGCAATAAACCAGCCAGCCGGAAAGGGCGAG  
 CGCAGAAGTGGTCTGCAACTTTATCCGCTCCATCCAGTCTATTAAATTGTTGCCGGGA  
 AGCTAGAGTAAGTAGTCGCCAGTTAATAGTTGCGCAACGTTGTTGCCATTGCTACAG  
 GCATCGTGGTGTACGCTCGCTGGTATGGCTTCTCAGCTCCGGTCCAAACGA  
 TCAAGGCAGTTACATGATCCCCATGTTGTGCAAAAAGCGGTTAGCTCCTCGGTCC  
 TCCGATCGTGTACAGTAAGTTGGCCGCAGTGTATCACTCATGGTTATGGCAGCAC  
 TGCATAATTCTCTTACTGTCTGACGCCATCCGTAAGATGCTTTCTGTGACTGGTGAGTAC  
 TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTGCCCGCGTC  
 AACACGGGATAATAACCGGCCACATAGCAGAACCTTAAAGTGTCTCATCATTGGAAAAC  
 GTTCTCGGGCGAAAACCTCAAGGATCTTACCGCTGTTGAGATCCAGTCGATGTA  
 CCCACTCGTGCACCCAACTGATCTCAGCATCTTACTTCAACCAGCGTTCTGGGTG  
 AGCAAAAACAGGAAGGCAAAATGCCGAAAAAAGGAATAAGGGCGACACGGAAATGTT  
 GAATACTCATACTCTTCCCTTTCAATATTATTGAAGCATTATCAGGGTTATTGTCTC  
 ATGACATTAACCTATAAAATAGGCAGT

**FIG.\_ 11C-2**

## (1) C12ScFas Survival construct

**C12ScFas:** epsilon-cFas(CD95)-Ires-Hygro-BGH PolyA put into C12s vector backwards so that no leaky transcription happens through the cmv promoter.

TGCTTATTGTCTCCAAATCCTCCCCCTGCTGTCCCTGCCACCCCCAGAAATAGAACCTACTCAGACAA

FIG. 12A

FIG. 12B

AACCCGGCTTCTTAACTCTCGGAGATGCTTATTAGTACCTTAACTGTGGCCAGCAAGCA

FIG. - 12C

FIG. 12D

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## (2) Ahhh: Survival construct

## 2.) Ahhh: 'epsilon-cFas' (CD8 or mLyt2)-Ires-Hygro-BGHpolyA also in C12s backwards

atcacgaggcccttgcgtttcaagaacagctttgctcttaggatttcttaatacataccaaactcaataatccaaatataaaagc  
 atttgacttgttctatgcccctagttataatagtaatcaattacggggtcatttagttcatagcccatatatggaggttccg  
 cgttacataacttacggtaatggccctggctgaccggccaaacggaccggccatgggtcaataatgggtcaatgggtatg  
 ttccatagtaacggccaaataggactttccattgacgtcaatgggtatattacggtaaacttgcctggcatatgcccaggta  
 catcaaggatgtatcatatgccaaggtaacggccatggcttacttgcgttacttgcgttacttgcgttacttgcgttacttgc  
 catgacccatggactttccattgacgttacttgcgttacttgcgttacttgcgttacttgcgttacttgcgttacttgc  
 agtacatcaatggggatggatggatggatggatggatggatggatggatggatggatggatggatggatggatggatggat  
 ttttgccacaaaatcaacgggactttccaaatgtcgtaacaactcccaaccccaaccccaaccccaaccccaaccccaaccc  
 acgggttctatataaggcaggctcaataaaaggcaggctcaataaggcaggctcaataaggcaggctcaataaggcaggctca  
 gagttgggggttgcgttacttgcgttacttgcgttacttgcgttacttgcgttacttgcgttacttgcgttacttgcgtt  
 tctccctgtgactgtgattgactaccccgctcaggcggttttcattgggggttgcgttacttgcgttacttgcgttacttgc  
 ggaccaccggacc  
 ttatgcgcccgtcggtacttagttacttagttacttagttacttagttacttagttacttagttacttagttacttagtt  
 cacccggccgcaaccctgggagacgtcccgaggacttgcgttcccttagaggaggatatgtgggttctggtagggacgg  
 tcgtttttggactctttggcaccccccttagaggaggatatgtgggttctggtagggacggatgttttttttttttttt  
 cgccctccgtctgaattttggcttcgggttttcgggttttcgggttttcgggttttcgggttttcgggttttcgggttt  
 tggtctgtgtgtactgtgttt  
 cttaggtcactggaaagatgtcgaggcgatcgctcacaaccctttaacgtcggttggccggagacggccacccatcacc  
 gctctggcggaaatggccaaaccttcaaggcccttttgcgttcccttacccatcggtggggatggggatggggatgggg  
 atcaagggttttcgggttttcgggttttcgggttttcgggttttcgggttttcgggttttcgggttttcgggttttcgg  
 cccctccctgggttttcgggttttcgggttttcgggttttcgggttttcgggttttcgggttttcgggttttcgggttt  
 aacctccctgggttttcgggttttcgggttttcgggttttcgggttttcgggttttcgggttttcgggttttcgggttt  
 gagatcttataatggggcacccccggcccttgcgttaaacttccctgacccctgacatgacaaggatttacttcc  
 ccaagctcactttacaggctctacttagtccaggacacggatgtggggagacccatccaaagaacaaactgg  
 accggccgggttaccccttaccccttaccccttaccccttaccccttaccccttaccccttaccccttaccccttaccc  
 cgtggaaaaggacccttacacaggccggccatcccttagacttcccttagacttcccttagacttcccttagacttcc  
 cccacccacccatcccttagacttcccttagacttcccttagacttcccttagacttcccttagacttcccttagacttcc  
 TGCTTATTGGTCTCCAAATCCTCCCTTGCTGTCCTGCCACCCCCACCCCCAGAATAATGACACCTACTCAGACAA  
 TGGATGCAATTCCCTCATTTATTAGGAAAGGACAGTGGGAGTGGCACCTTCCAGGGTCAAGGAAGGGCACGGGGGG  
 GCAAACAACAGATGGCTGGCAACTAGAAGGCACAGTCGAGGTCTAGCTTGCCAAACCTACAGGTGGGTCTTTCATTCCC

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 FIG.\_13A

GAGTGGACACCTGTGGAGAAAGGCAAAGTGGATGTCAGTAAGACCAATAGGTGCCATTATCAGAAACGCAAGAGTCTTCT  
CTGTCTCGACAAGCCCAAGTTCTTAAACCTGTCTCCCTTAACCTGTCTTGTAAACCTTGATACTTACCTGCCAGTGCCCTCAGC

FIG. - 13B

TTTGCAAGGCATGGAAAATACATAACTGAGAATAGAGAAGGTCAGATCAAGGTGGAAACAGATGGAACAGGCAATAAA  
AGAGCCACAAACCCCTCACTCGGGGCCAGTCCTCCGATTGACTGAGTGGCCGGTACCCGTATCCAAATAAACCT  
CTTGCAGTTGCATCCGACTTGCATGTATCAAATAATTAAATTGGTTTTCTTAAGTTACATTAATGGCCATAGttcGTAAT  
TCTTTCAcatgcaGCACTGTTCCCTGCTGTGAAATTGTTATCCGCTCACAACTACGAGCCGAAGCATAAAAGTGT  
CATGGTCATAGCTGTTCCTGCTGTGAAATTGTTATCCGCTCACAACTACGAGCCGAAGCATAAAAGTGT  
AAGGCCTGGGTGCCCTAATGAGTGAGCTAACATCACATTAAATTGGCTTCCAGTCGGAAACCT  
GTCGTGCCAGCTGCATTAAATGAATCGGCCAACGGCGGGAGAGGGTGTGCGTATTGGCCGCTTCCGCTTCTCGC  
TCAGCTGACTCGGTGCCCTGGCTCGGGGAGGGTATCAGCTCACTCAAGGGCTAAATACGGTTATCCACA  
GAATCAGGGATAACGCAGGAAGAACATGTAAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAGGGCCGGTGTGCT  
GGCGTTTCCATAGGCTCCGCCCTGACGAGCATCACAAATGACGGCTCAAGTCAGAGGTGGCAAACCCGACAG  
GACTATAAAGATAACCGGGGTTCCTGGAAAGCTCCCTGCTGGGGCTCTCCGTTACGGGATAAC  
CTGTCCGCCCTTCCCTGGGAAGGGTAGGTTCTAGGCTCACGGTGTAGGTATCTCAGTTGGTAACTATCGTCTTGAGT  
TCGGCTCCAAGCTGGCTGTGCAAGAACCCCCGGTCAAGCCGACTGGCAAGGAGGGTAACTGGTATCCGGCTTATCGTCTTGAGT  
CCAAACCCGGCTAAAGACACCACTTATCGGCCAGCAAGGGGACTGGTAACTGGTATCCGGCTTATCGTCTTGAGT

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GCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAACACTAGAAGGACAGTATTGGTATCTGGCTCTGCTGAAGCC  
 AGTACCTCGGAAAAGAGTTGGTAGCTCTTGATCCGGAAACAAACCCGGCTGGTAGGGGTGTTTTGTTGCA  
 AGCAGCAGATTACGGCAGAAAAAGGATCTCAAGAAGATCCTTGATCTTCTACGGGTCTGACGGCTCAGTGGAAC  
 GAAACTCACGTTAAGGGATTGGTCATGAGATTATCAAAAAGGATCTCACCTAGATCCTTTAAATTAAAATGAAG  
 TTTGGCAAAATCAATCTAAAGTATATATGAGTAACCTTGTCAGTTACCAATGCTTAATCAGTGAGGGCACCTATCT  
 CAGGGATCTGTCTATCCATAGTTGCCGTGACTCCCGTGTAGATAACTACGATAACCCGGGGCTTACCA  
 TCTGGCCCCAGTGTGCAATGATAACCGGAGACCCACGGCTCACCGGCTCCAGATTATCAGCAATAACCGCCAGCCGG  
 AAGGGCCGAGCCAGAACTTGCTCCCTGCAAACCTTATCCGCTCCATCCAGTCTATTAAATTGTTGCCGGAAAGCTAGAGTAA  
 GTAGTTGCGCAGTTAATAGTTGCGCAACGTTGCCATTGCTACAGGCATCAGGCTCGTGTAGCTGGTATG  
 GCTTCATTCAAGCTCCGGTCCAAACGATCAAGGGAGTTACATGATCCCCATGTTGTGCAAAAAGGGTTAGCTCCTT  
 CGTCCTCCGATCGTGTCAAGAAGTAAGTGGCGCAGTGTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTA  
 CTGTCATGCCATCCGTAAGATGCTTCTGTGACTGGTGGagtactcaaccaagtcatctgagaataagtgtatggcgca  
 ccgagttgtcttgcccggtcaacacggataataccggccacatagcagaactttaaaagtgtctcatcattggaaa  
 acgtttttccggggggggaaactctcaaggatcttacggatccgttggatcccgactcgtggcaccctcaact  
 gatcttcagcatctttacttccaccaggcggttttgcggatggatggcaaaaacaggaaaggcaaaaaggaaata  
 agggcagacacggaaaatgttgataactcatctttcaattatgtaaaggatttcagggttattgtctcat  
 gacattaacctataaaaataggcgt

FIG.\_ 13D